Interional Application No PCT/EP2004/006222

| A. CLASSIFIC   | CATION OF SUBJECT MATTER C12N15/86   |  |  |
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| According to I   | nternational Patent Classification (IPC) or to both national classification a  | nd IPC   |  |
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| Minimum doc<br>IPC 7   | C12N   | •  |  |
|  | on searched other than minimum documentation to the extent that such d   | ocuments are included in the fields sea  | rched  |
| Documentation  | on searched office the transfer of the search of the searc |  | €  |
| Steetronic da  | ta base consulted during the international search (name of data base an  | d, where practical, search terms used)   |  |
| EPO-Int  | ternal, BIOSIS, MEDLINE, WPI Data, PAJ   | · ·  |  |
|  |  |  |  |
| C. DOCUME  | NTS CONSIDERED TO BE RELEVANT  | t nassages   | Relevant to claim No.  |
| Category °   | Citation of document, with indication, where appropriate, of the relevan   |  |  |
| X  | GAO GUANGPING ET AL: "Adeno-associviruses undergo substantial evolutions primates during natural infections PROCEEDINGS OF THE NATIONAL ACADEM SCIENCES OF THE UNITED STATES, vol. 100, no. 10, 13 May 2003 (2003-05-13), pages 60 XP002255703   | ."<br>Y OF   | 1-3,7  |
|  | May 13 2003 2003 ISSN: 0027-8424 page 6083, left-hand column, last paragraph - right-hand column, par  | agraph   |  |
| X FL   | urther documents are listed in the continuation of box C.  | X Patent family members are liste  | d in annex.  |
| "A" docu<br>con<br>"E" earlic<br>filin<br>"L" docu<br>whi<br>cita<br>"O" docu<br>oth<br>"P" docu<br>late | ment defining the general state of the art which is not sidered to be of particular relevance or document but published on or after the international grate of the may throw doubts on priority claim(s) or lich is cited to establish the publication date or another ation or other special reason (as specified) the publication or other special reason (as specified)   | or priority date and not in conflict we cited to understand the principle or invention  X" decument of particular relevance; the cannot be considered novel or can involve an inventive step when the cannot be considered to involve and document of particular relevance; the cannot be considered to involve and document is combined with one or ments, such combination being obtain the art.  *A" document member of the same pater.  Date of mailing of the international | theory underlying the e claimed invention not be considered to document is taken alone e claimed invention inventive step when the more other such docu- vious to a person skilled |
|  | 13 December 2004   | 0 3. 05  | . 2005   |
| Name a   | nd mailing address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2  NL - 2280 HV Rijswijk  Tel. (+31-70) 340-2040, Tx. 31 651 epo nt,  Fax: (+31-70) 340-3016   | Niebuhr-Ebel,  | (  |

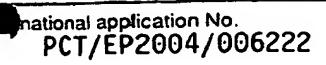
International Application No PCT/EP2004/006222

|           |   | PCT/EP2004/ |                    |
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| Continua  | ion) DOCUMENTS CONSIDERED TO BE RELEVANT  |             |                    |
| ategory * | Citation of document, with indication, where appropriate, of the relevant passages  | Rel         | evant to claim No. |
| X ·       | & DATABASE SWALL EMBL; 1 June 2003 (2003-06-01), GAO ET AL.: "Adeno-associated viruses undergo substantial evolution in primates during natural infections" XP002255706 Database accession no. Q808Y0 the whole document  |             | 1-3,7              |
| X<br>     | WO 02/053703 A (CHILDRENS HOSPITAL INC) 11 July 2002 (2002-07-11) "AAV vectors and methods" page 20; example 3; table 4 claims 4,6,7  |             | 1,6-10             |
| A         | CALDWELL ELIZABETH E O ET AL: "Importance of specific amino acids in protein binding sites for heparin and heparan sulfate." INTERNATIONAL JOURNAL OF BIOCHEMISTRY & CELL BIOLOGY, vol. 28, no. 2, 1996, pages 203-216, XP002255704 ISSN: 1357-2725 abstract page 206, left-hand column, paragraph 2 - right-hand column, paragraph 1 |             | 1-10               |
| P,X       | KERN A ET AL: "Identification of a heparin-binding motif on adeno-associated virus type 2 capsids."  JOURNAL OF VIROLOGY, vol. 77, no. 20, October 2003 (2003-10), pages 11072-11081, XP002310361 ISSN: 0022-538X the whole document  |             | 1-10               |
| P,X       | WO 03/054197 A (BUENING HILDEGARD; HUTTNER NADJA (DE); MEDIGENE AG (DE); PERABO LU)  3 July 2003 (2003-07-03)  "A library of modified structural genes or capsid modified particles useful for the identification of viral clones with desired cell tropism"  |             | 1,6-10             |
|           | page 35; example 5<br>claims 13,41,42; table 1  | •           | •                  |
|           | -/  |             |                    |
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International Application No PCT/EP2004/006222

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|                         | Ition) DOCUMENTS CONSIDERED TO BE RELEVANT  | PLIZEPZOU             |      |
|-------------------------|---|-----------------------|------|
| .(Continua<br>ategory * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |      |
| <b>,</b> X              | OPIE SHAUN R ET AL: "Identification of amino acid residues in the capsid proteins of adeno-associated virus type 2 that contribute to heparan sulfate proteoglycan binding."  JOURNAL OF VIROLOGY, vol. 77, no. 12, 20 June 2003 (2003-06-20), pages 6995-7006, XP009018010 ISSN: 0022-538X |                       | 1-10 |
| ٠.                      | ISSN: 0022-538X<br>the whole document   | •                     |      |
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| Box II Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)   |
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| This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:   |
| 1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:   |
|  |
| Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: |
| 3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).  |
| Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)   |
| This International Searching Authority found multiple inventions in this international application, as follows:  |
| see additional sheet   |
| 1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.  |
| 2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.  |
| .3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:                   |
|  |
| No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:           |
| 1-10   |
|  |
| Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.  |
|  |

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-10

Mutant R475A, a pharmaceutical composition containing said mutant and its use for gene therapy

2. claims: 1-10

Mutant R484A, supra

3. claims: 1-10

Mutant R484E, supra-

4. claims: 1-10

Mutant R487A, supra

5. claims: 1-10

Mutant R487E, supra

6. claims: 1-10

Mutant K527A, supra

7. claims: 1-10

Mutant K532A, supra

8. claims: 1-10

Mutant R585E, supra

9. claims: 1-10

Mutant R588E, supra

10. claims: 1-10

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Due to the large number of combinatorial possibilities, the total number of inventions has not been determined. However, it is considered that each modification at a certain position and each combination of modifications at more than one position may constitute a separate invention.

ntormation on patent family members

PCT/EP2004/006222

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| Patent document cited in search report |   | Publication date |                      | Patent family member(s)                                  | Publication date                                     |
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| WO 02053703                            | A | 11-07-2002       | WO<br>US             | 02053703 A2<br>2002192823 A1                             | 11-07-2002<br>19-12 <b>-</b> 2002                    |
| WO 03054197                            | Α | 03-07-2003       | AU<br>CA<br>WO<br>EP | 2002352261 A1<br>2468882 A1<br>03054197 A2<br>1456383 A2 | 09-07-2003<br>03-07-2003<br>03-07-2003<br>15-09-2004 |